Reconsideration is requested with respect to the rejection under 35 USC 112, first paragraph.

According to the statement of rejection, in vivo targeting is highly unpredictable. However, no support for this allegation is given. In order to sustain a rejection for lack of enablement under §112, first paragraph, the PTO must cite evidence in support of any allegations of non-enablement, in addition to explaining *why* it doubts the truth of statements of enablement made in the specification. *In re Sichert*, 196 USPQ 209 (CCPA 1977). Accordingly, in the absence of the requisite evidence, the §112, ¶1, rejection cannot be maintained.

Reconsideration is requested with respect to the rejection under 35 USC 102(b) for alleged anticipation based on Crooke and with respect to the rejection under 35 USC 102(e) for alleged anticipation based on Baracini.

For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp*. To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis added*). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

There is no teaching or suggestion in Crooke for a rational design of antisense oligonucleotides, such as presently claimed. Crooke tested some oligonucleotides for their toxicity. Although Crooke synthesized oligonucleotides that might fall within the scope of the antisense oligonucleotides produced according to the presently claimed method, this does not anticipate the method. Crooke neither teaches nor suggests designing an antisense oligonucleotide using the criteria recited in the present claims. That is, the "designing" step is absent from the reference. There being a limitation on the present claims absent from the cited reference, anticipation is negated. *Kolster Speedsteel A B, supra.*

Baracini discloses oligonucleotides. Some of them fall within the scope of antisense oligonucleotides produced by the presently claimed method, but others do not. Sequences ID Nos. 1, 2, and 11 comprise "runs" of guanosine. Baracini even discloses (column 8, line 35) that such runs of contiguous nucleotides are preferred.

In prior art, people often simply tested for the proliferation of cells upon treatment with antisense oligonucleotides. Specific and unspecific could not be distinguished, therefore, even oligonucleotides having a number of 4 or 5 contiguous guanosines were considered effective. The instant inventors revealed that unspecific toxic effects can be avoided if elements of consecutive G's are avoided. This teaching cannot be derived from any of other documents.

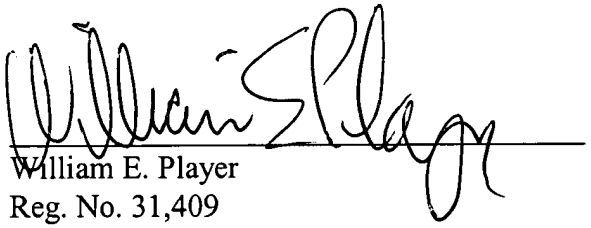
That the number of consecutive G's (GGG or longer) is important, is demonstrated in example 1 of the instant specification. These oligonucleotides are not effective and toxic. In prior art, these contiguous guanosine containing antisense sequences were even considered to be helpful.

Attached, hereto, is an article from Burgess et al. The article points out that such antisense oligonucleotides have therapeutic potential. In contrast thereto, the inventors of the present application found that such oligonucleotides should be avoided.

Favorable action is requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By: 

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